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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: WOLFFE et al.	Examiner: R. Akhavan
Application No.: 10/084,826	Group Art Unit: 1636
Filed: October 24, 2001	Confirmation No.: 4340
For: TARGETED MODIFICATION OF CHROMATIN STRUCTURE	

APPEAL BRIEF

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2/16/06 Michelle Hobson
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APPEAL BRIEF

Mail Stop Appeal Brief
Commissioner for Patents
Alexandria, VA 22313

Sir:

INTRODUCTION

Appellants submit one copy of this brief on appeal in accordance with Section 41.37 (69 Fed. Reg. 49962, Aug 2004). All examined claims were finally rejected under 35 U.S.C. § 112, 1st paragraph, written description in a Final Office Action mailed September 14, 2005. A Notice of Appeal, Request for Pre-Appeal Brief Conference and Pre-Appeal Brief Argument was filed on November 16, 2005. A Notice of Panel Decision from Pre-Appeal Brief Review was mailed on December 15, 2005. Thus, an Appeal Brief was initially due on January 16, 2006.

Appellants request a one-month extension of time and enclose the appropriate fee, making an Appeal Brief due by February 16, 2006. Accordingly, this Appeal Brief is timely filed.

I. REAL PARTY IN INTEREST

Sangamo BioSciences, Inc., the assignee of record of the above-referenced patent application is the real party in interest in this matter.

II. RELATED APPEALS AND INTERFERENCES

Appellants filed an Appeal Brief in USSN 09/844,508, the parent of the present application, on March 10, 2005. Subsequent to the filing of that Brief, USSN 09/844,508 was allowed and will issue on February 21, 2006. Thus, no decision in the parent case (USSN 09/844,508) has been rendered by the Board of Appeals and Interferences.

III. STATUS OF THE CLAIMS

Claims 1-7, 10-36 and 40-73 are currently pending in the above-referenced case (hereinafter "the application"). Claims 34-36 and 40-43 have been examined. The application was originally filed on October 21, 2001 as a continuation-in-part of USSN 09/844,508 with claims 1 to 73. In a Preliminary Amendment filed April 9, 2003, claims 1, 34, 40, 44, 65, 67, 72 and 73 were amended, and claims 8, 9, and 37-39 were canceled. Following a Restriction Requirement dated September 15, 2004, claims 1-7, 10-14, 19-33, and 44-73 were withdrawn from consideration and claims 34-36 and 40-43 were examined. Claim 40 was amended in a paper filed April 19, 2005. No pending claims were amended after mailing of the Final Office Action on September 14, 2005. Accordingly, claims 1-7, 10-36 and 40-73 are pending shown in the Claims Appendix and examined claims 34-36 and 40-43 remain rejected under 35 U.S.C. § 112, 1st paragraph (written description).

IV. STATUS OF THE AMENDMENTS

The examined claims have not been amended after the mailing of the Final Office Action. Thus, claims 34-36 and 40-43 remained rejected for the reasons set forth in the Final Office Action mailed September 14, 2005.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The subject matter of examined claims 34-36 and 40-43 relates to fusion molecules (page 12, line 29) comprising (a) a DNA-binding domain (page 12, line 30; page 30, line 4 to page 32, line 21); and (b) an enzymatic component of a chromatin remodeling complex or a functional fragment thereof (page 32, line 23 to page 42, line 18). The enzymatic component of a chromatin remodeling complex or functional fragment thereof is selected from the group consisting of a histone methyl transferase, a histone kinase, a histone phosphatase, a histone ubiquitinating enzyme, a histone de-ubiquitinating enzyme and a histone protease (page 2, lines 24 to 30 and page 33, lines 13-23).

The fusion molecules may be, for example, a fusion polypeptide (page 6, line 24). Fusion polypeptides may include, for example, a DNA binding domain that comprises a zinc finger protein (ZFP) (page 6, lines 1-3). The DNA binding domain of the fusion polypeptide can bind to a target site in a gene encoding a product selected from the group consisting of vascular endothelial growth factor, erythropoietin, androgen receptor, PPAR γ2, p16, p53, pRb, dystrophin and e-cadherin (page 7, lines 4-9).

The subject matter of the examined claims also relates to polynucleotides encoding these fusion polypeptides (page 6, lines 29-30 and page 10, lines 20-22) as well as cells comprising the fusion polypeptides and/or the polynucleotides encoding these fusion molecules (page 6, line 30 to page 7, line 1).

VI. GROUNDS OF REJECTION

1. Examined claims 34-36 and 40-43 stand rejected under 35 U.S.C. § 112, 1st paragraph as allegedly not adequately described by the as-filed specification.

VII. ARGUMENTS

1. The Office Has Not Properly Assessed the Disclosure of the As-Filed Specification

It is axiomatic that any written description inquiry is dependent on the particular facts of the case. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim*, 191 USPQ 90 (CCPA 1976). The facts that must be taken into account include the disclosure as a whole and the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lukach*, 169 USPQ 795, 796 (CCPA 1971); *In re Lange*, 209 USPQ 288 (CCPA 1981). That which is not new need not be described in detail. *See, e.g., Capon v. Eshhar* 76 USPQ2d 1078 (Fed. Cir. 2005).

Thus, the proper standard for determining satisfaction of the written description involves reviewing the disclosure as a whole, taken together with available knowledge, to determine whether the specification as-filed evinces possession of the claimed subject matter to the skilled artisan. Any written description inquiry that does not completely or accurately assess the particular disclosure of the specification and determine the state of the field is necessarily flawed.

Throughout prosecution of the instant case, the Office has failed to consider both the disclosure of the as-filed specification as a whole and the knowledge possessed by the skilled artisan at the time of filing. Instead, the Office appears to have considered only the Examples and Figures, and has failed to acknowledge the known state of the field (*e.g.*, as evidenced by published sequence information). Consequently, the adequacy of Appellants' written description has not been properly assessed and the rejection cannot be sustained.

The Office's assessment that the specification in question "discloses" only that which is exemplified can be found throughout both the non-Final and Final Office Actions (*see,* Final Office Action, page 3, last paragraph; page 4, first paragraph; page 8, second paragraph; page 9, first and second paragraphs (emphasis added)):

> The specification **discloses** a fusion polypeptide comprising a DBD [DNA-binding domain] that recognizes target sequence in the human VEGF gene, which

> is alternatively fused to BAF155, MBD1, MBD2, MDB3, DNMT, and KRAB (e.g., Figs. 6-7; Examples 2-13).
>
> The **disclosed** embodiments are directed exclusively to DNA modification, while the claims encompass a genus that includes both DNA or histone covalent modification. There are no embodiments **disclosed** of structures or functional fragment [*sic*] of structures that function to covalently modify histones.
>
> Notably the specification **identifies** structures that are non-enzymatic components of chromatin remodeling complexes (*e.g.,* MBD1, MBD2, MBD3, DNMT and KRAB; Examples 2-13, Figs. 6-7).
>
> In other words, not a single embodiment is **disclosed** of a fusion molecule structure that functions to covalently modify histones.
>
> In addition, the specification does not **identify** a single fusion molecule where the DNA binding domain is a non-protein (e.g., chemical agent or nuclei [*sic*] acid), but that is linked to an enzymatic component or functional fragment thereof, and that effectuates chromatin remodeling.

Time and time again, the Office ignores what is disclosed in the background, summary, detailed description and original claims, asserting instead that only the Examples and Figures constitute "adequate" disclosure.

However, when the actual disclosure and state of the art regarding Appellants' particular case are properly assessed, it is clear that the written description requirement has been met, and possession of the claimed subject matter has been conveyed.

Indeed, as repeatedly noted, the as-filed specification contains literal disclosure of known enzymatic components of chromatin remodeling complexes (*see, e.g.,* Background as well as pages 32-42 describing, in detail, enzymatic chromatin remodeling complexes that covalently modify histones) as well as known non-protein DNA binding domains (*see, e.g.,* page 5, lines 29-30; page 30, lines 5-23 describing non-protein DBDs such as triplex-forming nucleic acids, intercalators, antibiotics, and minor groove binders). Moreover, the as-filed specification literally discloses the novel claimed fusion molecules (*see, e.g.,* pages 7, lines 23-31; page 8, lines 1-9 and 18-21; pages 32-42). Simply put, there is literal disclosure in the specification of <u>every</u> embodiment encompassed by the claims.

In the case on appeal, the Office has taken into account only that which is exemplified. When viewed as a whole, Appellants' disclosure literally discloses every embodiment falling within the scope of the claims. Not only have Appellants shown possession of the individual components of the claimed fusion molecules (*see, e.g.,* Background and pages 32-42 detailing known chromatin remodeling complexes that covalently modify histones and page 30 detailing non-protein DNA binding proteins), they have evinced possession of that which is new – namely fusing a DNA binding domain to a histone methyl transferase, a histone kinase, a histone phosphatase, a histone ubiquitinating enzyme, a histone de-ubiquitinating enzyme or a histone protease in order to obtain targeted remodeling of chromatin.

Disclosure, not exemplification, is what is relevant to the written description inquiry and, in the case at hand, there is ample disclosure demonstrating possession of the claimed genus. To require exemplification of actual, multiple embodiments is contrary to all established precedent and the rejection cannot stand.

2. Possession of the Claimed Genus Has Been Established

As noted above and throughout prosecution (including the Pre-Appeal Brief Conference Arguments), the as-filed specification contains ample description regarding the claimed fusion molecules. This description includes literal description of the known components (known histone modifying enzymes and known DNA-binding molecules) as well as proper citations to references indicating what was known to those skilled in the art (again, the particular enzymatic components of the recited chromatin remodeling complexes and various known DNA binding domains). More importantly, the specification teaches that which is new, *i.e.,* how to fuse these known DNA binding domains to known chromatin remodeling proteins to form the novel and unobvious fusion molecules of the claims.

(a) The As-Filed Specification Describes the Claimed Genus Throughout Its Scope

As noted above, the Office has repeatedly asserted that no structures of non-protein fusion molecules or enzymatic chromatin remodeling complexes are described and that the art

cannot supplement the allegedly inadequate disclosure (*see, e.g.,* pages 5 and 7 of the Final Office Action):

> The specification does not provide any structures comprising non-protein fusion molecules (e.g., genus of molecules encompassed by claim 40). Furthermore, knowledge in the art does [*sic*][1] supplement the instant disclosure's omission of a sufficient description. For example, "In contrast to the relative wealth of information about the large number of acetyltransferases and deacetylases, relatively little is known about the enzymes that generate other histone modifications." [citation omitted] ...
>
> Given the enormous breadth of the fusion molecules, comprising DNA binding domains and enzymatic components or chromatin remodeling complexes, including functional fragments thereof, encompassed by the rejected claims, including non-protein-protein fusion molecules, and given the limited description in the instant specification of such fusion molecules, the skilled artisan would not be able to envision a sufficient number of specific embodiments to described [*sic*] the broadly claimed genus. Therefore, the skilled artisan would reasonably have concluded that applicants were not in possession of the claimed invention.
>
> The instant specification provides insufficient description of the essential/critical structures encompassed by the broadly claimed genus of fusion molecules.

In fact, the Examiner errs in asserting both that the specification is defective and, moreover, that art available at the time of filing cannot be used to supplement the disclosure.

As repeatedly noted, the as-filed specification amply discloses structures of non-protein DNA binding domains (*e.g.,* page 30 of the as-filed specification). In addition, the as-filed specification also provides structures of various chromatin remodeling proteins as claimed, including, for example, histone kinases (*see, e.g.,* page 3, line 23 and citing Sassone-Corsi et al. (1999)) and histone methyltransferases (*see, e.g.,* page 2, line 31 citing Rea et al. (2000) and the detailed description on pages 32-42, particularly page 33, of proteins such as Su(Var)3-9 that were known at the time of filing to be histone methyltransferases).

Furthermore, contrary to the Examiner's assertion, it is completely proper to supplement the specification's disclosure using references available at the time of filing. *See, e.g., In re*

[1] Appellants assume "does not" was intended

Lukach, 169 USPQ 795, 796 (CCPA 1971); *In re Lange*, 209 USPQ 288 (CCPA 1981). Indeed, a patent specification need not recite and preferably omits that which is not new. *See, e.g., Loom Co. v. Higgins,* 105 U.S. 580, 585-86 (1882); *In re Wands,* 858 F.2d 731 (Fed. Cir. 1988) and *In re Gay,* 309 F.2d 769, 774 (CCPA 1962) pointing out that "not every last detail [of an invention need] be described [in a specification], else patent specifications would turn into production specification, which they were never intended to be." See also *Capon v. Eshhar* 76 USPQ2d 1078 (Fed. Cir. 2005) for a recent explication of this doctrine in the biotechnology context.

In the case on appeal, structures of various exemplary histone modifying proteins were known at the time of filing and citations to these proteins are contained in the as-filed specification (*see, e.g.,* Sassone-Corsi et al. (1999) and Rea et al. (2000) cited in the specification and IDS and disclosing the structure of histone kinases and histone methyltransferases). Indeed, SNF-1, which is described in detail in the specification, was known at the time of filing to be a histone kinase (*see, also,* Lo et al. (2001) *Science* 293(5532):1142-1146). Additional histone modifying enzymes (and their sequences) were available to the public well before the application on appeal was filed in 2001. By way of example, histone phosphatases such as PP2A were described as early as 1988 (*see, e.g.,* Usui et al. (1988) *J. Biol. Chem.* 263:3752-3761 and Zhao (1994) *Biochem Mol Biol Int* 34(5):1027-1033). Histone proteases, histone ubiquinases and histone ubiquitinases were described in the mid-1990s (*see, e.g.,* Goffeau et al. (1996) *Science* 274:546-547; Kaiser et al. (1994) *J. Biol. Chem.* 269:8797-8802; Cai (1999) *Proc Nat'l Acad Sci USA* 96(6):2828-2833).

Thus, those of skill in the art would have been aware of the histone modifying enzymes described in the previous paragraph, as of the filing date. Appellants have also provided evidence that the claimed DNA-binding domains, both protein and non-protein, were known in the art at the time of filing. *See* Appellants' Response dated April 19, 2005 at pages 13-14. It is unreasonable to assert that this known information must be set forth *verbatim* in the specification.

It is also unreasonable to assert that the claims must recite some kind of "essential" or "critical" structure encompassed by the claims. (*See,* page 7 of the Final Office Action,

reproduced above). The nature of the claimed fusion molecules is such that they cannot be adequately presented by recitation of a particular structure, even though the as-filed specification provides ample description in this regard. Broad, pioneering claims are not *per se* inadequately described. In fact, all the critical features of the claimed, pioneering fusion molecules have been described.

Furthermore, Appellants submit that the allegation that "relatively little" is known about certain histone modifying enzymes is irrelevant to the instant written description inquiry. First of all, the examiner has not specified what is not known about these enzymes. Their structure and/or function may be well characterized but "relatively little known" about such things as their mechanism of action.

In sum, given the disclosure of the specification, one of skill in the art would clearly envision the allegedly enormous breadth of the claims.[2] Indeed, the Examiner has envisioned such embodiments. *See, e.g.*, page 4, first paragraph of the Final Office Action, noting that the specification points out that "chromatin remodeling can occur through DNA or histone covalent modification" as encompassed by the claims.[3]

(b) The Case Law Supports a Finding that the As-Filed Specification Describes the Claimed Subject Matter

Because literal description of numerous representative fusion molecules is present in the specification as filed, the Examiner cannot rely on *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991), *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961 (Fed. Cir. 1997) and *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) to try to show that the particular case on appeal does not adequately describe the claimed subject matter.

In *Vas-Cath,* the Federal Circuit determined that the written description was in fact satisfied because the drawings did not have to exclude all diameters other than those within the

[2] Appellants note also that the breadth of a claim has no relationship to the adequacy of its written description

[3] Page 5 of the Final Office Action provides a specific example of the Examiner's vision of a claimed embodiment. Therein it is stated that Pham *et al.* show histone ubiquitin[ating] activity for $TAF_{II}250$. Thus, a fusion between $TAF_{II}250$ and a DNA-binding domain represents an embodiment that has been envisioned by the Examiner.

claimed range. *Vas-Cath,* at 1119. Therefore, *Vas-Cath* actually supports a finding of adequate written description where the specification includes a disclosure of all possible fusion molecules.

In *Lockwood,* the written description requirement was analyzed in order to determine if the patentee was entitled to the benefit of a previous filing date for claims directed to particular automated sales terminals. The Federal Circuit reiterated the fact-dependent nature of the written description inquiry and, on the particular facts, held that possession was not shown because that which was claimed in the patent was not disclosed in an earlier application. *Lockwood,* at 1964. However, *Lockwood* contains a completely different fact-pattern than that found in the case on appeal (priority claim vs. adequacy of original disclosure/claims). Lockwood's claims failed to satisfy the written description requirement because an intervening application was held not to describe an terminal containing a video disc player. By contrast, and unlike *Lockwood,* Appellants' as-filed specification contains literal description of the claimed subject matter.

Thus, under both *Lockwood* and *Vas-Cath,* Appellants have demonstrated possession of the claimed subject matter, thereby fully satisfying the written description requirement.

As with *Lockwood*, the fact-pattern in *Eli Lilly* is completely different than that of the case on appeal. In *Lilly,* the claims were directed to novel insulin-encoding sequences which were not disclosed in (or known prior to the filing of) the as-filed specification. In contrast, the pending claims are directed to novel fusion molecules that are literally described in the specification and whose components were described in the specification and known in the art. Therefore, the findings in *Eli Lilly* have no bearing on the facts of the present application.

Federal Circuit decisions that are more germane to the case on appeal are *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 54 USPQ2d 1227 (Fed. Cir. 2000) and *Capon v. Eshhar* 76 USPQ2d 1078 (Fed. Cir. 2005). Appellants note that both *Union Oil* and *Capon* are more recent than *Vas-Cath, Lockwood* and *Eli Lilly.*

In *Union Oil v. Atlantic Richfield*, the Federal Circuit made clear that specification need **not** describe the exact chemical composition of every claimed combination, adding that neither the Patent Act nor case law requires such detailed disclosure (*see, Union Oil,* at 1223):

> Appellant refiners assert that the specification does not describe the exact chemical component of each combination that falls within the range claims of the

> '393 patent. However, neither the Patent Act nor the case of this court requires such detailed disclosure. ...
>
> The inquiry for adequate written description simply does not depend on a particular claim format, but rather on whether the patent's description would show those of ordinary skill in ... art that the inventors possessed the claimed invention at the time of filing.

In *Capon v. Esshar,* the Federal Circuit completely rejected the notion that the specification must describe information (*e.g.,* sequence data) that is either known or can readily be determined based on scientific facts (*Capon* at page 1085, emphasis added):

> The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. ...
>
> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution.

The holding in *Capon* in particularly relevant to the instant case because the fact pattern in *Capon* is highly analogous to the fact pattern in the case at issue. In *Capon*, the Federal Circuit held that the precise sequence of a chimeric (fusion) antibody need **not** be described because the components were well known.

The Examiner's assertion in the case on appeal that Appellants are required to disclose multiple examples of particular fusion molecules, when each of the components (DNA binding domains that bind to particular target sites and enzymatic portion of the recited chromatin remodeling complexes), as well as methods of making fusion proteins, were well known and described in the specification as-filed, is inconsistent with the requirements of the first paragraph of Section 112.

Contrary to the assertions in the Final Office Action, it is totally proper (and persuasive), as the Federal Circuit reiterated in *Capon*, to argue that each component of the fusion molecule was well known and described, methods for fusion are well known in the art and described in the specification and, hence, the claimed fusions are described. Appellants have clearly evinced possession of the components of the claimed fusion molecules and, accordingly, have satisfied the written description requirement.

Moreover, Appellants also amply describe that which is new, *i.e.,* fusing a DNA binding domain to one of the chromatin remodeling proteins recited in the claims. Thus, the disclosure of the specification as filed more than satisfies the written description requirement with the respect to the pending claims; and the notion that the specification provides "sufficient information in order for a person of skill in the art to construct such a product," but somehow fails to describe that product is completely at odds with not only *Capon* but with every case, rule and guideline relating to the written description requirement.

Plainly, clear description is present in the original claims and specification, and the written description requirement has therefore been satisfied. Appellants have shown possession of the claimed molecules at the time of filing – clearly and unmistakably. As result, the rejection cannot be sustained.

CONCLUSION

For the reasons stated above, Appellants respectfully submit that the pending claims are clearly described in the specification. Accordingly, Appellants request that the rejection of the claims on appeal be reversed, and that the application be remanded to the Examiner so that the appealed claims can proceed to allowance.

Respectfully submitted,

Date: February 16, 2006

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CLAIMS ON APPEAL

1. (withdrawn) A method for modifying a region of interest in cellular chromatin, the method comprising the step of contacting the cellular chromatin with the fusion molecule according to claim 40, thereby modifying the region of interest.

2. (withdrawn) The method of claim 1, wherein the cellular chromatin is present in a plant cell.

3. (withdrawn) The method of claim 1, wherein the cellular chromatin is present in an animal cell.

4. (withdrawn) The method of claim 3, wherein the cell is a human cell.

5. (withdrawn) The method of claim 1, wherein the fusion molecule is a fusion polypeptide.

6. (withdrawn) The method of claim 1, wherein the DNA-binding domain comprises a zinc finger DNA-binding domain.

7. (withdrawn) The method of claim 1, wherein the DNA-binding domain is a triplex-forming nucleic acid or a minor groove binder.

8. (canceled)

9. (canceled)

10. (withdrawn) The method of claim 1, wherein chromatin modification facilitates detection of a sequence of interest.

11. (withdrawn) The method of claim 10, wherein the sequence of interest comprises a single nucleotide polymorphism.

12. (withdrawn) The method of claim 1, wherein chromatin modification facilitates activation of a gene of interest.

13. (withdrawn) The method of claim 1, wherein chromatin modification facilitates repression of a gene of interest.

14. (withdrawn) The method of claim 1, wherein chromatin modification facilitates recombination between an exogenous nucleic acid and cellular chromatin.

15. (withdrawn) The method of claim 5, wherein the method further comprises the step of contacting a cell with a polynucleotide encoding the fusion polypeptide, wherein the fusion polypeptide is expressed in the cell.

16. (withdrawn) The method of claim 1, further comprising the step of identifying an accessible region in the cellular chromatin, wherein the fusion molecule binds to a target site in the accessible region.

17. (withdrawn) The method of claim 1, wherein the region of interest comprises a gene.

18. (withdrawn) The method of claim 17, wherein the gene encodes a product selected from the group consisting of vascular endothelial growth factor, erythropoietin, androgen receptor, PPAR-γ2, p16, p53, pRb, dystrophin and e-cadherin.

19. (withdrawn) The method of claim 1, further comprising the step of contacting the cellular chromatin with a second molecule.

20. (withdrawn) The method of claim 19, wherein the second molecule is a transcriptional regulatory protein.

21. (withdrawn) The method of claim 19, wherein the second molecule is a fusion molecule.

22. (withdrawn) The method of claim 21, wherein the second molecule is a fusion polypeptide.

23. (withdrawn) The method of claim 21, wherein the second molecule comprises a zinc finger DNA-binding domain.

24. (withdrawn) The method of claim 23, wherein the second molecule further comprises a transcriptional activation domain.

25. (withdrawn) The method of claim 23, wherein the second molecule further comprises a transcriptional repression domain.

26. (withdrawn) The method of claim 23, wherein the second molecule further comprises a polypeptide sequence selected from the group consisting of a histone acetyl transferase, a histone deacetylase, a functional fragment of a histone acetyl transferase, and a functional fragment of a histone deacetylase.

27. (withdrawn) The method of claim 19, further comprising the step of contacting the cellular chromatin with a third molecule.

28. (withdrawn) The method of claim 27, wherein the third molecule is a transcriptional regulatory protein.

29. (withdrawn) The method of claim 27,wherein the third molecule is a fusion molecule.

30. (withdrawn) The method of claim 29,wherein the third molecule is a fusion polypeptide.

31. (withdrawn) The method of claim 29, wherein the third molecule comprises a zinc finger DNA-binding domain.

32. (withdrawn) The method of claim 31, wherein the third molecule further comprises a transcriptional activation domain.

33. (withdrawn) The method of claim 31, wherein the third molecule further comprises a transcriptional repression domain.

34. (previously presented) The fusion molecule of claim 40, wherein the fusion molecule is a fusion polypeptide.

35. (original) The polypeptide of claim 34, wherein the DNA-binding domain is a zinc finger DNA binding domain.

36. (original) The polypeptide of claim 34, wherein the DNA binding domain binds to a target site in a gene encoding a product selected from the group consisting of vascular endothelial growth factor, erythropoietin, androgen receptor, PPAR-γ2, p16, p53, pRb, dystrophin and e-cadherin.

37. (canceled)

38. (canceled)

39. (canceled)

40. (previously presented) A fusion molecule comprising

(a) a DNA-binding domain; and

(b) an enzymatic component of a chromatin remodeling complex or a functional fragment thereof, wherein the enzymatic component of a chromatin remodeling complex or functional fragment thereof is selected from the group consisting of a histone methyl transferase, a histone kinase, a histone phosphatase, a histone ubiquitinating enzyme, a histone de-ubiquitinating enzyme and a histone protease.

41. (original) A polynucleotide encoding the fusion polypeptide of claim 34.

42. (original) A cell comprising the fusion polypeptide of claim 34.

43. (original) A cell comprising the polynucleotide of claim 41.

44. (withdrawn) A method for modulating expression of a gene, the method comprising the steps of:

a) contacting cellular chromatin with the fusion molecule according to claim 40; and

b) further contacting the cellular chromatin with a second molecule that binds to a target site in the gene and modulates expression of the gene.

45. (withdrawn) The method of claim 44, wherein modulation comprises activation of expression of the gene.

46. (withdrawn) The method of claim 44, wherein modulation comprises repression of expression of the gene.

47. (withdrawn) The method of claim 44 wherein the DNA-binding domain of the first fusion molecule comprises a zinc finger DNA-binding domain.

48. (withdrawn) The method of claim 44 wherein the second molecule is a polypeptide.

49. (withdrawn) The method of claim 48 wherein the second molecule comprises a zinc finger DNA-binding domain.

50. (withdrawn) The method of claim 49, wherein the second molecule further comprises an activation domain.

51. (withdrawn) The method of claim 49, wherein the second molecule further comprises a repression domain.

52. (withdrawn) The method of claim 44 wherein the second molecule is a transcription factor.

53. (withdrawn) The method of claim 52 wherein the transcription factor is an exogenous molecule.

54. (withdrawn) The method of claim 52 wherein the transcription factor is an endogenous molecule.

55. (withdrawn) The method of claim 44 wherein the first fusion molecule and the second molecule each comprise a zinc finger DNA-binding domain.

56. (withdrawn) The method of claim 44 wherein a plurality of first fusion molecules is contacted with cellular chromatin, wherein each of the first fusion molecules binds to a distinct binding site.

57. (withdrawn) The method of claim 44, wherein a plurality of second molecules is contacted with cellular chromatin, wherein each of the second molecules binds to a distinct target site.

58. (withdrawn) The method of claim 56 wherein at least one of the first fusion molecules comprises a zinc finger DNA-binding domain.

59. (withdrawn) The method of claim 57 wherein at least one of the second molecules comprises a zinc finger DNA-binding domain.

60. (withdrawn) The method of claim 44 wherein the expression of a plurality of genes is modulated.

61. (withdrawn) The method of claim 60 wherein a plurality of first fusion molecules is contacted with cellular chromatin, wherein each of the first fusion molecules binds to a distinct binding site.

62. (withdrawn) The method of claim 61 wherein at least one of the first fusion molecules is a zinc finger fusion polypeptide.

63. (withdrawn) The method of claim 60, wherein a plurality of second molecules is contacted with cellular chromatin, wherein each of the second molecules binds to a distinct binding site.

64. (withdrawn) The method of claim 63 wherein at least one of the second molecules is a zinc finger fusion polypeptide.

65. (withdrawn) The method of claim 60 wherein the first fusion molecule binds to two or more of the plurality of genes.

66. (withdrawn) The method of claim 65 wherein the first fusion molecule is a zinc finger fusion polypeptide.

67. (withdrawn) The method of claim 60 wherein the second molecule binds to two or more of the plurality of genes.

68. (withdrawn) The method of claim 67 wherein the second molecule is a zinc finger fusion polypeptide.

69. (withdrawn) The method of claim 1, wherein chromatin modification results in the generation of an accessible region in the cellular chromatin.

70. (withdrawn) The method of claim 69, wherein generation of the accessible region facilitates binding of an exogenous molecule.

71. (withdrawn) The method of claim 70, wherein the exogenous molecule is selected from the group consisting of polypeptides, nucleic acids, small molecule therapeutics, minor groove binders, major groove binders and intercalators.

72. (withdrawn) A method for producing the fusion polypeptide of claim 34, the method comprising the step of expressing the polynucleotide of claim 41 in a suitable host cell.

73. (withdrawn) A method for binding an exogenous molecule to a binding site, wherein the binding site is located within a region of interest in cellular chromatin, wherein the method comprises:

(a) contacting cellular chromatin with a fusion molecule according to claim 40; and

(b) introducing the exogenous molecule into the cell;

whereby the exogenous molecule binds to the binding site.

RELATED PROCEEDINGS APPENDIX

As noted on page 2 of the Appeal Brief, Appellants have filed an Appeal Brief in USSN 09/844,508, which is the parent of the present application. As of filing this Appeal Brief, no decision in the Appeal of the parent case has been rendered.